Dastidar, A. G., Harries, I., Pontecorboli, G., Bruno, V. D., De Garate, E., Moret, C., Baritussio, A., Johnson, T. W., McAlindon, E., & Bucciarelli-Ducci, C. (2019). Native T1 mapping to detect extent of acute and chronic myocardial infarction: comparison with late gadolinium enhancement technique. *International Journal of Cardiovascular Imaging*, *35*(3), 517-527. https://doi.org/10.1007/s10554-018-1467-1

NATIVE T1 MAPPING TO DETECT EXTENT OF ACUTE AND CHRONIC MYOCARDIAL INFARCTION: COMPARISON WITH LATE GADOLINIUM ENHANCEMENT TECHNIQUE

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Brief title: Non contrast assessment of myocardial viability by T1 mapping

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Abstract

Aim:

Investigate whether native-T1 mapping can assess the transmural extent of myocardial infarction(TEI) thereby differentiating viable from non-viable myocardium without the use of gadolinium-contrast in both acute and chronic myocardial infarction(aMI and cMI).

METHODS:

60patients (30 cMI>1year and 30 aMI day2 STEMI) and 20 healthy-controls underwent 1.5T CMR to assess left ventricular function(cine), native-T1 mapping(MOLLI sequence 5(3)3, motion-corrected) and the presence and TEI from late gadolinium enhancement(LGE) images. Segments with <75% TEI was considered viable. Gold-standard LGE-TEI was compared with corresponding segmental native-T1.

RESULTS:

Segmental native-T1 correlated significantly with TEI(R= 0.74,p<0.001 in cMI and R=0.57,p<0.001 in aMI)**.** Native-T1 differentiated segments with no LGE(1031±31ms), LGE positive but viable(1103±57ms) and LGE positive but non-viable(1206±118ms) in cMI(p<0.01). It also differentiated segments with no LGE(1054±65m), LGE positive but viable(1135±73ms) and LGE positive but non-viable(1168±71ms) in aMI(p<0.01). ROC analysis demonstrated excellent accuracy of native-T1 mapping compared to LGE-TEI(AUC-0.88,p <0.001 in cMI, vs AUC –0.83,p<0.001 in aMI). Native-T1 performed better in cMI than aMI(p<0.01). In cMI a segmental T1 threshold of 1085ms differentiated viable from non-viable segments with a sensitivity 88% and specificity of 88% whereas a T1 of 1110ms differentiated viable from nonviable with 79% sensitivity and 79% specificity in aMI.

CONCLUSIONS:

Native-T1 mapping correlates significantly with TEI thereby differentiating between normal, viable, and non-viable myocardium with distinctive T1 profiles in aMI and cMI. Native T1-mapping to detect MI performed better in cMI compared to aMI due to absence of myocardial oedema. Native-T1 mapping holds promise for viability assessment without the need for gadolinium-contrast agent.

KEYWORDS:

Viability, T1 mapping, Cardiovascular Magnetic Resonance, Myocardial infarction

Introduction

Acute myocardial infarction leads to reversible (viable/stunned) and irreversible(non-viable) myocardial injury, even after successful coronary reperfusion. Early recognition of viable myocardium after a myocardial infarction(MI) is of clinical relevance as the affected segments have the potential for recovery. Targeted revascularization of viable myocardium improves clinical outcomes. Hence viability assessment is a key aspect in the management of ischaemic heart disease (IHD). Late gadolinium enhancement (LGE) CMR is increasingly used in clinical practice as a viability assessment tool (1,2). LGE viability assessment is performed by analyzing the extent of scar thickness, with a myocardial segment ≥75% transmurality deemed mostly non viable. The transmural extent of infarct (TEI) assessed by LGE has been shown to be inversely related to functional recovery after reperfusion (3,4). LGE imaging requires administration of gadolinium-based contrast agents. The use of these contrast agents is limited in patients with moderate to severe renal dysfunction due to the potential risk of nephrogenic systemic fibrosis.(5) In addition there have been several reports of gadolinium-based deposits in the central nervous system structures following repeated use of gadolinium contrast, whose clinical meaning is still uncertain. (6) An alternative viability imaging method that might obviate the use of contrast-agents is desirable.

Myocardial T1 mapping is emerging as a novel non-contrast CMR imaging tool in the assessment of non-IHD and IHD (7). Native T1 mapping technique is highly sensitive to changes in myocardial tissue, thereby providing excellent tissue characterization obviating for the need for contrast administration. Kali et al. looked at diagnostic accuracy of T1-mapping in the detection of overall transmurality in chronic MI using a thresholding-based detection.(8) We tested the hypothesis that native segmental T1 mapping can assess the TEI

thereby differentiating between viable and non-viable myocardium in IHD without the use of gadolinium contrast.

Aim:

The aim of the study was to compare the performance of native segmental T1 mapping in quantifying the TEI/myocardial scarring with LGE in chronic as well as acute MI patients using a 1.5T CMR.

Methods:

Study population

60 patients with myocardial infarction were recruited: 30 successfully re-perfused STEMI patients (mean age 61±10years and 80% males) scanned at day 2 and 30 chronic MI patients (>1year after MI) (mean age 67±10years and 80% males). All patients were diagnosed with MI according to guidelines. (9,10) Exclusion criteria were: general contraindications to CMR, chronic atrial fibrillation, renal impairment with eGFR <30, and cardiogenic shock. 20 age- and sex-matched healthy volunteers served as control (all free of cardiovascular disease). The study was approved by the local Institutional Research and Innovation department. All patients gave informed written consent. Findings were compared with 20 healthy volunteers with no previous medical history (mean age 59±16yrs, 75% male).

Image acquisition

Patients underwent CMR scans on a 1.5-T scanner (Magnetom Avanto, Siemens) with a standard 8-channel matrix coil configuration.

The imaging protocol consisted of three long-axis (four-, three-, and two-chamber view) and a full stack of short-axis steady-state free precession cine images as previously described. (11) This was followed by the acquisition of three short-axis slices (basal, mid-cavity, and apical) by using T1mapping sequence (details of the sequence provided below). Subsequently, acquisition of the same three short-axis slices (basal, mid-cavity, and apical) was repeated by using a segmented inversion-recovery gradient-echo sequence (IR-GRE) 1–3 minutes after the intravenous administration of 0.1 mmol/kg of gadobutrol (Gadovist; Bayer Schering Pharma, Berlin-Wedding, Germany) (early gadolinium enhancement EGE). Late gadolinium enhancement (LGE) images were acquired 15-20 minutes after contrast agent injection in the three long-axis and the full stack of short-axis views. (12) In acute MI cohort T2weighted STIR(short tau inversion recovery) images were acquired on short-axis planes covering the entire left ventricle prior to gadolinium administration.

Late gadolinium enhancement imaging

Images were acquired at least 15 min following administration of 0.1 mmol/kg gadobutrol. LGE images were obtained using an inversion recovery prepared breath-hold gradient-echo technique. Typical image parameters were TR 700 ms, TE 4.33 ms; matrix 256 × 256; flip angle 30°; slice thickness 8.0 mm, no interslice gap, and voxel size 1.7 × 1.4 × 8 mm. The inversion time was progressively optimized to null normal myocardium (typical values, 250–350 ms). Images were acquired on both the long- and short-axis planes covering the entire left ventricle. Each slice was obtained during a breath-hold of 10–15 s depending on the patient's heart rate

T1 mapping sequence

Myocardial T1-mapping was performed using the modified Look-Locker inversion recovery (MOLLI) sequence 5(3)3 (Siemens Healthcare, Germany). The 5(3)3 MOLLI protocol was used to ensure more-complete recovery of the inversion pulse at higher heart rates by acquiring a set of images for at least 5 seconds after the first inversion pulse, followed by a 3-second pause and then acquiring a set of images after the second inversion pulse for at least 3 seconds. The acquisition parameters were: pixel bandwidth, 977 Hz/pixel; echo time=1.12 ms; flip angle=35 degrees; matrix=256×144; and 8 mm slice thickness. A nonlinear least-square curve fitting and motion correction were performed at different inversion times with the set of images acquired to generate a pixel-wise colored T1 map by the scanner.(13)

T2w STIR

A breath-hold black-blood segmented turbo spin echo sequence was adopted for T2w STIR imaging, using a triple inversion recovery preparation module in order to suppress signal from flowing blood as well as from fat, with surface coil normalization. (14) Typical imaging parameters were TR 2 R-to-R intervals, TE 75 ms, flip angle 90°, TI 170 ms, slice thickness 8 mm, no interslice gap, field of view 340–400 mm, matrix 208 × 256, and a voxel size of 2.3 × 1.4 × 8 mm. Each slice was obtained during a breath-hold of 10–15 s depending on the patient's heart rate. To accommodate poor breath-holders, turbo factor was increased as necessary.

Image analysis

Argus software (Siemens, Germany) was used for the quantification of LV volumes and ejection fraction (EF) (15). Segmental TEI was assessed by contouring the area of LGE and

dividing it by the area of the whole segment using full width at half maximum(FWHM) technique using CVI42 software (Circle Cardiovascular Imaging, Calgary, Alberta, Canada). A scar transmurality scale of 0-4 was used for the 16 AHA segment (0=no scar, 1= 1-24%, 2=25-49%, 3=50-74%s and 4=≥75% scar thickness). A scar transmurality grade of 3 or less (<75% TEI) was deemed viable. (3,16) Observer blinded to the LGE data(AGD) drew regions of interest within the native T1 map in each of the American Heart Association (AHA) 16 segments in the short axis motion corrected maps using Argus software, adjusting for partial-voluming and/or artefact, as previously described. (17) **Figure 1** The LGE data was blinded for the T1 mapping analysis in order to test the hypothesis that T1 mapping can assess viability without the need of LGE. Images were randomized for analysis. In patients with acute MI, the hypointense areas in the LGE images (representing MVO), when present, were included in the contoured areas for the segment wise calculation of TEI. The infarct size was calculated from the LGE images by semi-automated software based analysis (FWHM) and expressed in % of the total LV volume. Another observer drew ROIs (GP) in the infarct core and remote myocardium in the T1 maps corresponding to the LGE image(unblinded). Remote myocardium was defined as myocardial tissue 180degree to the infarct with no evidence of hyperenhancement or myocardial oedema, as previously described.(18) Analysis was also done as per the coronary artery territory. Myocardial segments were assigned to coronary arteries as described in the AHA 16 segment model(excluding the apical cap), with 6 segments for the left anterior descending artery, 5 for the right coronary artery, and 5 for the left circumflex artery. (19) In each patient 'global native T1' was derived by taking the mean T1 of all 16 AHA segments. Images were suboptimal/non diagnostic if there was artefact or signal loss that interfered with the ability of the observers to interpret the image. This was observed in 3 patients but to overcome

the problem the sequences were repeated. In the final analysis no images were considered non-diagnostic.

Statistical analysis

Statistical analysis was performed using SPSS V.23 (Armonk, New York, USA: IBM Corp.) and R version 3.1.2 (R Core Team 2014). Categorical variables were analyzed using Fisher exact tests. Normally distributed continuous variables were expressed as mean±standard deviation and compared using unpaired Student t tests or one-way analysis of variance with Bonferroni post hoc correction for between-groups comparisons, as appropriate. Continuous variables that were not normally distributed were compared by Kruskal–Wallis tests. R-values quoted are for Pearson's correlation coefficient. The potential of quantitative T1-mapping to assess the TEI or viability on a segmental basis against the current gold standards of LGE were explored. The analysis was also performed as per each coronary artery territory. Interobserver (AGD and IH) and intraobserver (AGD) variability for segmental native T1 was assessed in 20 patients (10 acute MI and 10 chronic MI patients), and expressed as intraclass correlation coefficient (ICC) and 95% confidence interval.

Segmental analysis run a risk of class effect due to the potential of multiple samples from the same patient. To nullify the class-effect a series of generalized linear mixed effect models, with the random intercept for each person and for each segment, were performed to assess the association between T1 mapping and viability/LGE TEI. The models were used to account for the fact that different segments from the same patient or same segment location from different patients may not behave independently. These models were conducted for both acute and chronic MI assessments. Receiver operating characteristic

(ROC) analysis was performed to identify area under curve (diagnostic accuracy) of native T1 as a marker of TEI by using corresponding LGE scoring (LGE score >3) as the gold standard. Cut-off values of T1 relaxation times as a marker of viability were also calculated from the ROC curve. Statistical significance of the differences between ROC curves was assessed using the online calculator (www.vassarstats.net). To take into consideration potential within-subject interaction of segments, clustered ROC analysis was also conducted to assess the performance of native T1 to predict viability. Significance was defined as two-tailed $p<0.05$.

Results:

The demographic and the CMR characteristics of the healthy control and the patient cohort (60 MI patients- acute and chronic MI subgroups) are presented in **Table 1.** The mean age of the healthy volunteers was 57±13yrs and 75% were male. The mean age was significantly lower in the acute MI group (61±10yrs vs 67±10yrs, p=0.017) compared to the chronic MI group. In 5%(n=3) of patients the T1 maps had artefacts or signal. To overcome this problem, the mapping images were repeated. Out of the 960 segments analysed from patients with previous MI(acute and chronic), 286 segments had evidence of LGE. Sixteen of the 30 acute MI patients had microvascular obstruction (MVO) (53%).

Interobserver and intraobserver variability for segmental T1 measurement

There was excellent inter and intra-observer agreement for native segmental T1 measurement. The intraclass correlation coefficient (ICC) and 95% confidence interval were

0.968 (0.958-0.976) for interobserver and 0.992(0.967-0.998) for intraobserver agreement respectively**.**

Chronic MI

T1 mapping vs scar transmurality (TEI)-In patients with chronic MI, the segmental T1 correlated significantly with LGE TEI (R= 0.74, p<0.001). **Figure 2a.** The mean segmental T1 value for LGE negative segments (myocardial segments with no infarction) was 1,031±31ms, LGE positive but viable (scar grade 1-3): 1,103±57ms and LGE positive but non viable (scar grade 4): 1206±118ms. The mean segmental T1 in each of the 3 categories (no LGE, LGE positive but viable and LGE positive but non-viable) were significantly different on a pairwise comparison with Bonferroni correction (p<0.01). **Figure 2b** The mean native T1 in the infarct core and remote myocardium were 1171±76ms and 1005±19ms respectively. **Table 2**

When grouping the segments into coronary artery territories, the correlation between native T1 and LGE TEI for RCA, LCx and LAD territories were R=0.77, 0.80, 0.69 respectively(p<0.001). Figure 2c

T1 mapping as a marker of transmurality of infarction -Native T1 mapping showed excellent diagnostic accuracy in predicting transmural LGE≥75% - AUC-0.88(CI 0.77- 0.99,p <0.001). Figure 2d A cut-off of native T1 of 1,085ms differentiated viable from non-viable segments with 88% sensitivity and 88% specificity. Clustered ROC curve analysis showed that segmental T1 mapping had an AUC of 0.8338 (95% CI 0.7002-1.00) to predict viability.

Mixed effects model with random intercept - Generalized linear mixed effect models, with the random intercept to assess the association between native T1 and viability/TEI correcting for the class effect due to multiple segments from same person or same segment location. Presence of non viability was significantly associated with native T1 (Chi square

307.02, p < 0.01), increasing it by 131.9 ± 6.3ms (standard errors). TEI significantly affected T1 (Chi square 388.9, p< 0.01), increasing it by 2.07± 0.1ms (standard errors) for every percent increase in TE.

Acute MI

T1 mapping vs scar transmurality (TEI)- In patients with acute MI, the segmental T1 correlated significantly with LGE TEI with R= 0.57, p<0.001. **Figure 3a** The mean segmental T1 value for scar transmurality grade 0 (no LGE) was 1,054±65ms, LGE positive but viable (scar grade 1-3): 1,135±73ms and LGE positive but non viable (scar grade 4): 1,168±71ms. The mean segmental T1 in the 3 categories (no LGE, LGE positive but viable and LGE positive but non-viable) were significantly different on a pairwise comparison with Bonferroni correction (p<0.01). **Figure** 3b The mean native T1 in the infarct core and remote myocardium were 1308±71ms and 1054±65ms respectively **Table 2.**

When grouping the segments into coronary artery territories, the correlation between native T1 and LGE TEI for RCA, LCx and LAD territories were R=0.66, 0.57, 0.57 respectively(p<0.001). **Figure 3c**

T1 mapping as a marker of transmurality of infarction - ROC analysis of segmental native T1 in acute MI against gold standard LGE viability(>75%TEI) showed good diagnostic accuracy AUC-0.83(CI 0.78- 0.88, p<0.001). **Figure 3d.** A T1 threshold of 1110ms most optimally differentiated viable from non-viable segments with 79% sensitivity and 79% specificity. Clustered ROC curve analysis showed that segmental T1 mapping had an AUC of 0.8338 (95% CI 0.7587-0.9088) to predict viability.

Mixed effects model with random intercept -Presence of non viability was significantly associated with native T1 (Chi square 145.4, p < 0.01), increasing it by 100.1 ± 7.7ms (standard errors). TEI significantly affected native T1 (Chi square 206.1, p=< 0.01), increasing it by 1.5± 0.1ms (standard errors) for every percent increase in TEI.

T2w STIR area at risk (oedematous area) in acute MI- All the acute MI scans showed evidence of myocardial oedema in the infarct related artery territory. The area at risk (total area of oedema) in the acute MI was 31±12% of the total LV.

Global native T1

Global native T1 in normal vs affected - Global native T1 in normal healthy volunteers was compared with all patients with previous MI (acute and chronic). The mean global T1 in normal volunteers was 1028±28ms, which was significantly lower than patients with previous MI 1070±36ms, p<0.0001. The global native T1 in patients with acute MI was 1082±34ms (p<0.0001 vs normal volunteer), whereas for chronic MI it was 1058±34ms(p=0.002 vs normal volunteer). **Figure 4**

Global native T1 vs Infarct size - Global native T1 was compared with the infarct size. For the total cohort (n=60) it showed a good positive correlation r= 0.575, p<0.001. Subgroup analysis: the correlation was found to be excellent in chronic MI r=0.717, p<0.001 whereas for acute MI it was weakly significant r=0.365, p=0.048 (**Figure 5a).**

Global native T1 vs LV EF -Global native T1 was compared with the left ventricular ejection fraction. For the total cohort (n=60) it showed a significant inverse correlation r= -0.445, p<0.001. Subgroup analysis: the correlation was found to be statistically significant in chronic MI r=-0.596, p<0.001 but not in acute MI r=-0.291, p=0.118. **Figure 5b**

T1 mapping vs wall motion score vs wall thickness for the assessment of viability

Segmental native T1 was compared with segmental wall thickness and segmental wall motion score against gold standard LGE viability. ROC analysis of the 960 segments for viability assessment showed the highest diagnostic accuracy of T1 mapping (AUC - 0.9, 95%CI 0.87- 0.93, p <0.0001) when compared to wall motion score (AUC 0.837, p<0.0001, 95%CI 0.8-0.875), and segmental wall thickness (AUC 0.453, p=0.07, 95%CI 0.401-0.505).

Discussion

The study looked at the diagnostic performance of segmental T1 mapping as a marker of LGE TEI and myocardial viability in patients with previous MI (acute and chronic). Overall native segmental T1 mapping had an excellent diagnostic accuracy, in distinguishing viable from non-viable myocardium when using LGE ≥75% transmurality as a reference standard to define infarcted non-viable myocardium. Diagnostic accuracy was better when used in chronic MI (AUC -0.88) rather than acute MI (AUC -0.83). The clinical value of T1 mapping lies in the evaluation of myocardial scar extent, on a voxel-wise basis, without the need to use a contrast agent.

Myocardial infarction is a regional disease affecting parts of the myocardium supplied by the occluded/stenosed coronary artery. Segmental analysis as per the AHA nomenclature is the most widely used cardiac imaging technique in current clinical practice. The study was designed to look at the T1 profile in different LGE TEI. In a segment wise analysis for T1 there was a statistically significant positive correlation between LGE TEI and the native T1

values. The association of native T1 and viability/TEI remained significant even adjusting for segments from same patient bias as well as same segment locations from different patient bias using the mixed effect model with random intercepts.

The opportunity to correlate presence and potential extent of infarction/scarring without the use of a contrast agent is clinically attractive. The T1-mapping as a single criterion demonstrated around 88% sensitivity, specificity in differentiating viable from nonviable myocardium in chronic MI. Our results were similar to the study by Ferreira et al looking at the accuracy of T1-mapping in delineating the extent and patterns of acute myocarditis.(20) It may be possible in future to perform a contrast-free CMR protocol using cine and T1-mapping for the assessment of TEI.

Viability assessment is a common indication for CMR not only in chronic IHD but also in acute MI. The latest ESC guidelines on management of STEMI recommend viability assessment in an acute setting in selected cases (including in multivessel disease). (21) In addition to a chronic MI group our study included an acute MI group thereby giving an opportunity to delineate the native T1 findings in acute MI patients.

The study delineated a higher accuracy of native T1 in chronic MI compared to acute for the assessment of viability. The reason behind the lower performance of native T1 in acute MI is most likely due to its pathophysiologic difference with chronic MI. Acute MI is characterised by oedema, loss of cell membrane integrity, an inflammatory response, necrosis, micro-vascular obstruction (MVO) and haemorrhage whereas chronic MI by scar tissue/fibrosis in the extracellular space. Our study showed that the mean area at risk (oedematous area) in

acute MI was 31% of LV which was significantly higher than the mean infarct size (21% of LV). The myocardial oedema delineated may have impacted on the performance of T1 mapping in acute MI. T1 mapping is influenced by all of these characteristics however LGE is not (especially oedema). In acute phase even LGE based TEI have been shown to be inaccurate(22) and hence may pose a limitation as a marker of viability/functional recovery. Beek et al demonstrated that 25% of segments with 75% to 100% TEI in acute MI had functional improvement at 13 weeks. (23)

Our study was performed on 1.5T scanner but the results were comparable to the study by Kali et al (8) in which they reported the diagnostic accuracy of T1-mapping in the detection of transmurality in chronic MI. Our study included both acute and chronic MI, thereby helping to compare the native T1 mapping findings in the 2 groups. Our main aim was to assess the significance of segmental native T1 as a discriminator between viable and non-viable myocardium unlike the study by Kali et al where they compared the overall transmurality between LGE and T1 mapping using thresholding technique. The native T1 value trends in the different infarct characteristics in acute and chronic MI in our study were comparable to the case series published by Dall'Armelina et al, although the actual values were different as her study was performed on 3T and ours at 1.5T.(24) A further study on native T1 in acute MI by Dall'Armellina et al. showed a strongly positive correlation between T1 value and the LGE TEI, but they excluded segments with MVO in the analysis. (25) The aim of our study was to assess viability without the use of contrast. It is very difficult to accurately identify MVO based on the T1 mapping alone without LGE imaging. In the study by Bulluck et al the diagnostic accuracy of T1 maps to identify MVO was 79-81% (26). Hence

in our study design the segmental native T1 analysis was done blinded to LGE data without excluding MVO.

Overall global native T1 showed a significant positive correlation with infarct size and LV ejection fraction. However, when the analysis was done for the acute and chronic groups the correlation was stronger in chronic compared to acute MI. The global native T1 did not correlate with LVEF in acute MI, again this is likely due to the effect of MVO or intramyocardial haemorrhage which reduces the T1 relaxation time.

Our study was performed on a 1.5T scanner, which is the most widely used machine. We have also shown a significant correlation at an individual coronary territory level. The T1 analysis was done from the T1 maps which were available immediately on the scanner console with no need for further post-processing. Apical slices were not excluded from analysis unlike other similar studies on T1 mapping due to the potential for partial volume artefact. (27) Similar studies have often eliminated lateral wall infarcts due to off-resonance artefact, but this is less relevant at 1.5T compared to 3T. (27) Moreover, our study sample had infarcts in all the different coronary territories including the lateral wall (which we included) to reduce the selection bias and reflect real world practice, whilst most of previous studies mainly included LAD infarctions.

Study Limitations

This is a single centre, single vendor study with a limited sample size. However, our findings were highly statistically significant. Larger multicenter, multivendor studies are warranted to confirm this proof of concept study. TEI on LGE imaging was used as the reference standard for viability rather than functional recovery which was used in other studies. TEI <75% was

used as the marker of viability in keeping with contemporary clinical practice. The acute and chronic MI cohorts were completely separate in our study unlike other studies. However, the study design was specifically constructed to remove any repeat measure from the same patient bias. Peri-infarct grey-zone on LGE, which has been shown be associated with arrhythmic events, was not assessed. This may have explained the difference between acute and chronic MI.

Conclusions

Native T1 mapping correlates significantly with TEI thereby differentiating between normal, infarcted viable, and infarcted non-viable myocardium with distinctive T1 profiles in both chronic and acute MI. Native T1 mapping performed better in chronic MI compared to acute due to the absence of myocardial oedema and microvascular obstruction. T1 mapping holds promise for viability assessment without the need for gadolinium contrast agents.

Abbreviations

CMR: Cardiovascular magnetic resonance

LGE: Late gadolinium enhancement

TEI: Transmural extent of infarct

AHA: American Heart Association

LV: Left ventricular

MI: Myocardial infarction

STEMI: ST-elevation myocardial infarction

MVO: Microvascular obstruction

AUC: Area under curve

ROC: Receiver operating characteristic

Acknowledgments

We thank Mr Christopher Lawton, superintendent radiographer, and his team of specialist CMR radiographers from the Bristol Heart Institute for their expertise in performing the CMR studies.

Funding

This study was supported by the NIHR Biomedical Research Centre at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

AGD is funded by the David Telling Charitable Trust.

Authors' contributions

AGD and CBD conceived the study design. EM & CBD coordinated and performed the MOIST trial. AGD, GP, VDB, IH, EDG, CM and IE participated in the analysis of CMR. AGD, IH, GP and CBD helped to interpret the data and draft the manuscript. All authors read and approved the final manuscript.

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http://www.ncbi.nlm.nih.gov/pubmed/26264813

Figure legends:

Figure 1: CMR images from a 54 year old with acute transmural myocardial infarction in right coronary artery, 1a) T1 map of the short axis, 1b) Region of interest drawn in each of the segment with corresponding native T1 value (blinded to LGE image), 1c) LGE image in the short axis, 1d) T1 map of the corresponding short axis with region of interest in the remote myocardium and infarct core(unblended to LGE image)

Figure 2: a) Scatter plot: chronic MI cohort showing native T1 value vs the TEI, 2b) Bar diagram with error bar(SD): Chronic MI cohort showing segmental native T1 value in LGE negative, LGE positive with viability and LGE segments with non-viability 2c) Scatter plot: Correlation between segmental T1 and Transmural extent of Infarct – as per coronary artery territory in chronic MI 2d) ROC curve: Chronic MI cohort comparing segmental native T1 vs LGE viability

Figure 3: a) Scatter plot: Acute MI cohort showing native T1 value vs the LGE TEI, 3b) Bar diagram with error bar(SD): Acute MI cohort showing segmental native T1 value in LGE negative, LGE positive with viability and LGE segments with non-viability 3c) Scatter plot: Correlation between segmental T1 and Transmural extent of Infarct – as per coronary artery territory in acute MI 3d) ROC curve: Acute MI cohort comparing segmental native T1 vs LGE viability

Figure 4: Boxplot showing the global native T1 in acute MI cohort, chronic MI cohort and the normal healthy volunteer

Figure 5: a)Scatter plot showing the correlation between global T1 and infarct size, 4b) Scatter plot showing the correlation between global T1 and LV ejection fraction

Table:

Table 1: Demographic/CMR characteristics table

Table 2: Mean Native T1(in ms) in the LGE negative segments, LGE positive but viable segments, LGE positive non-viable segments, Infarct core and Remote myocardium

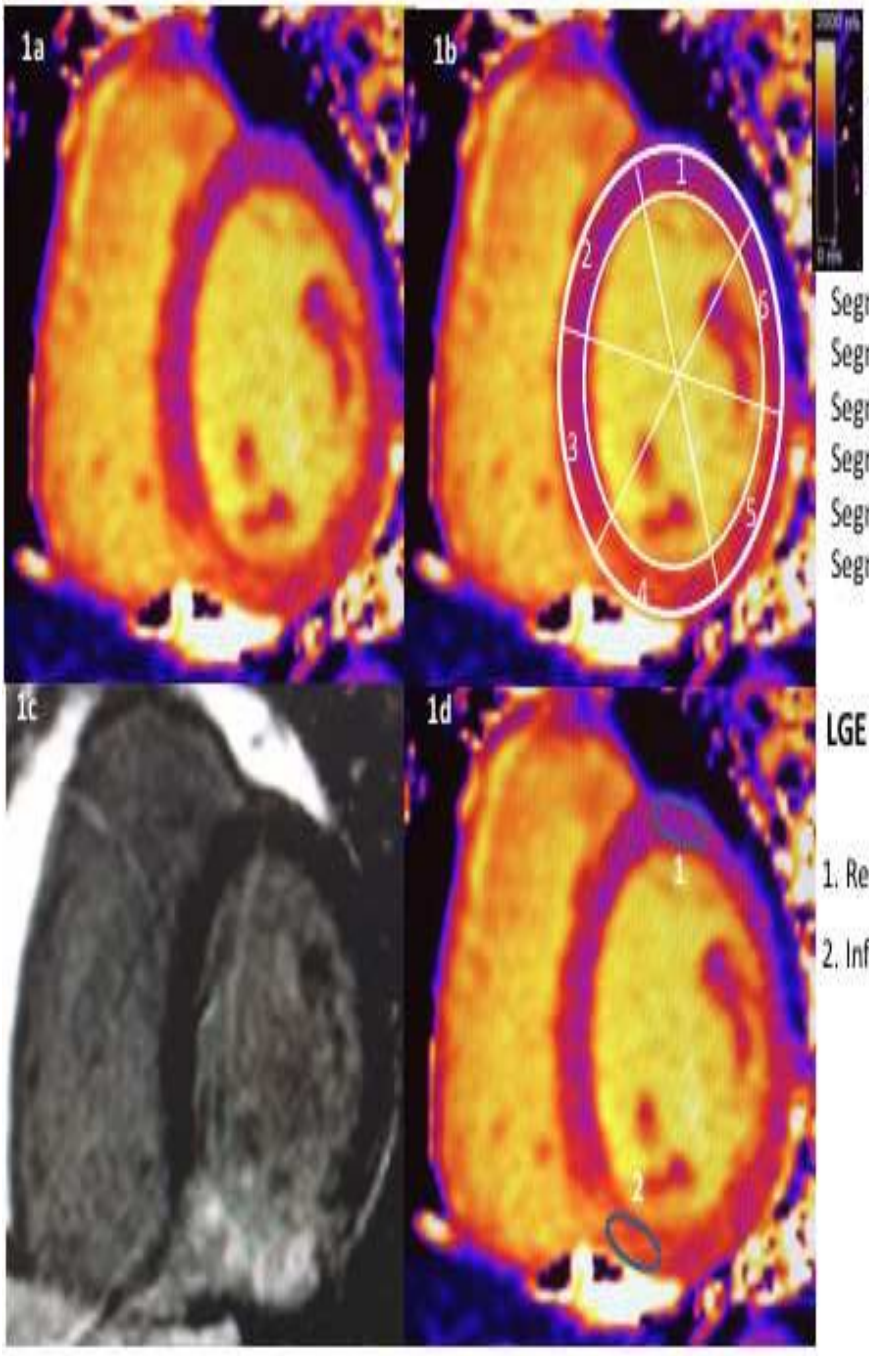
Table 1:

Characteristics	**Control (n=20)**	**Acute MI (n=30)**	**Chronic MI (n=30)**	**p-value (acute vs chronic)**
Age, years	57(±13)	61(±10)	67(±10)	0.017
Female Sex, %	25%	20%	20%	1.0
Smoking, %	-	27	17	0.356
Hypertension, %	-	43	53	0.447
Diabetes, %	-	10	23	0.171
CMR				
LV EF %	66(±7)	51(±9)	51(±13)	0.833
EDV ml	146(±35)	152(±29)	167(±56)	0.218
ESV ml	51(±18)	77(±26)	85(±48)	0.406
SV ml	95(±22)	75(±13)	83(±23)	0.144
Infarct size %	-	21(±10)	16(±12)	0.135

Table 2:

Category	LGE negative segments	LGE positive viable segments	LGE positive non-viable segments	Infarct core	Remote myocardium
Chronic MI Mean T1(ms) ±SD	1031±31	1103±57	1206±118	1171±76	1005±19
Acute MI Mean T1(ms) ±SD	1054±65	1135±73	1168±71	1308±71	1054±65

54 year old with acute transmural myocardial infarction in right coronary artery



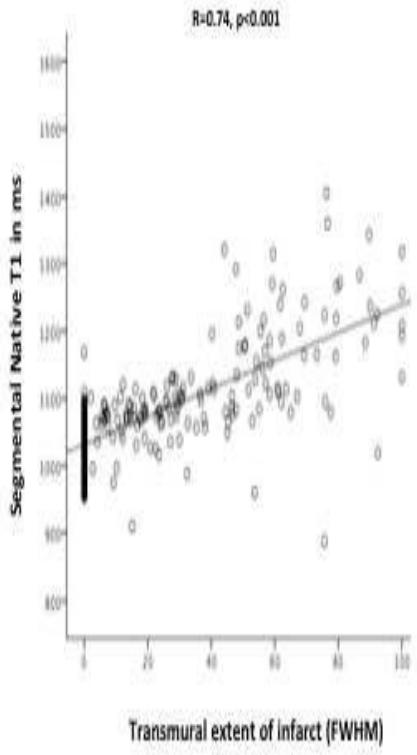
SEGMENTAL NATIVE T1

Segment 1 – 1008ms
Segment 2 - 1036ms
Segment 3 – 1064ms
Segment 4 – 1223ms
Segment 5 - 1100ms
Segment 6 – 1037ms

LGE IMAGE & NATIVE T1 MAP

1. Remote myocardium – 1001ms
2. Infarct core – 1254ms

2a



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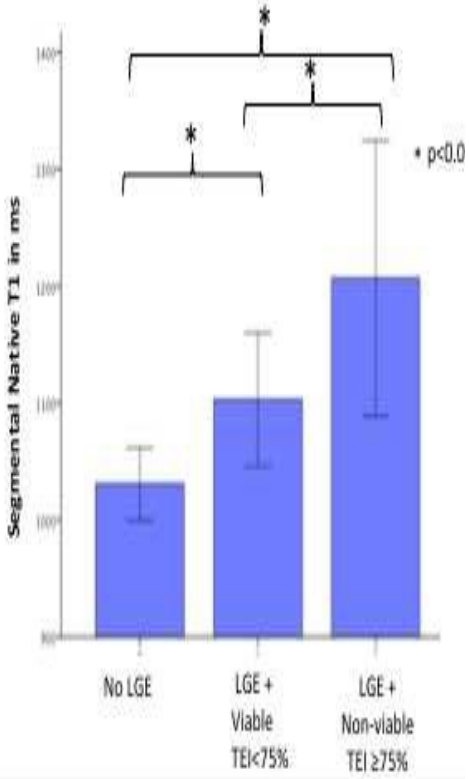

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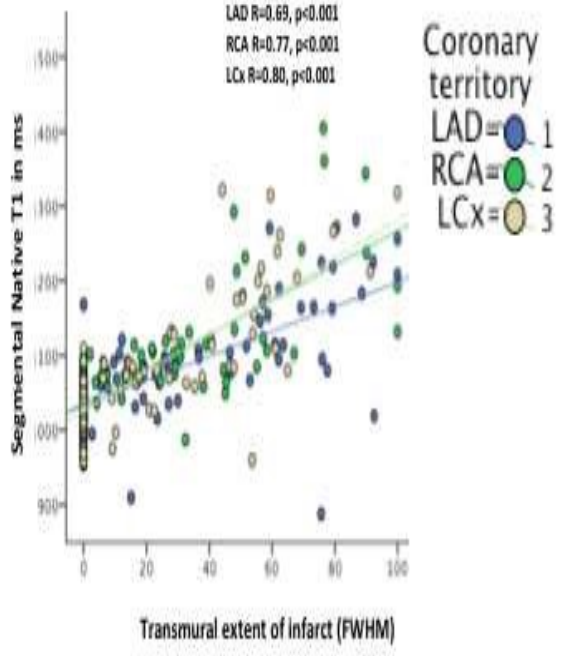

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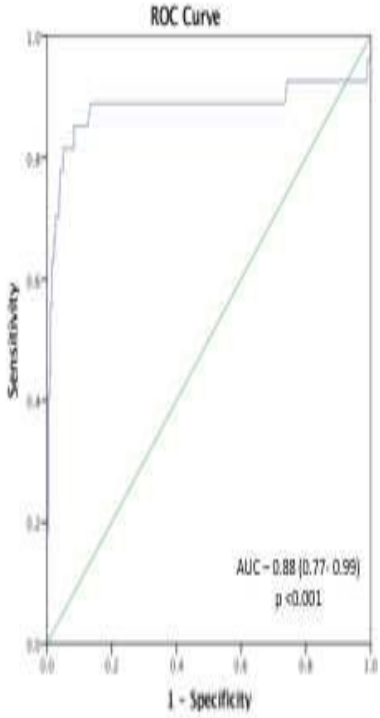
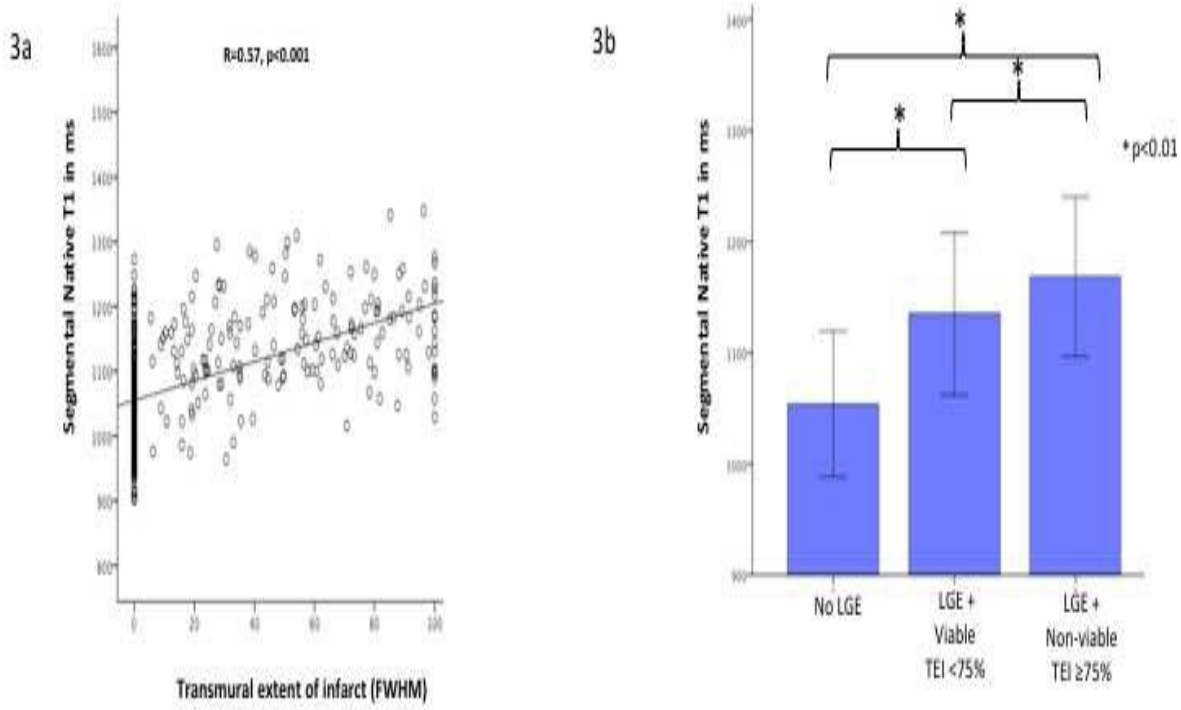
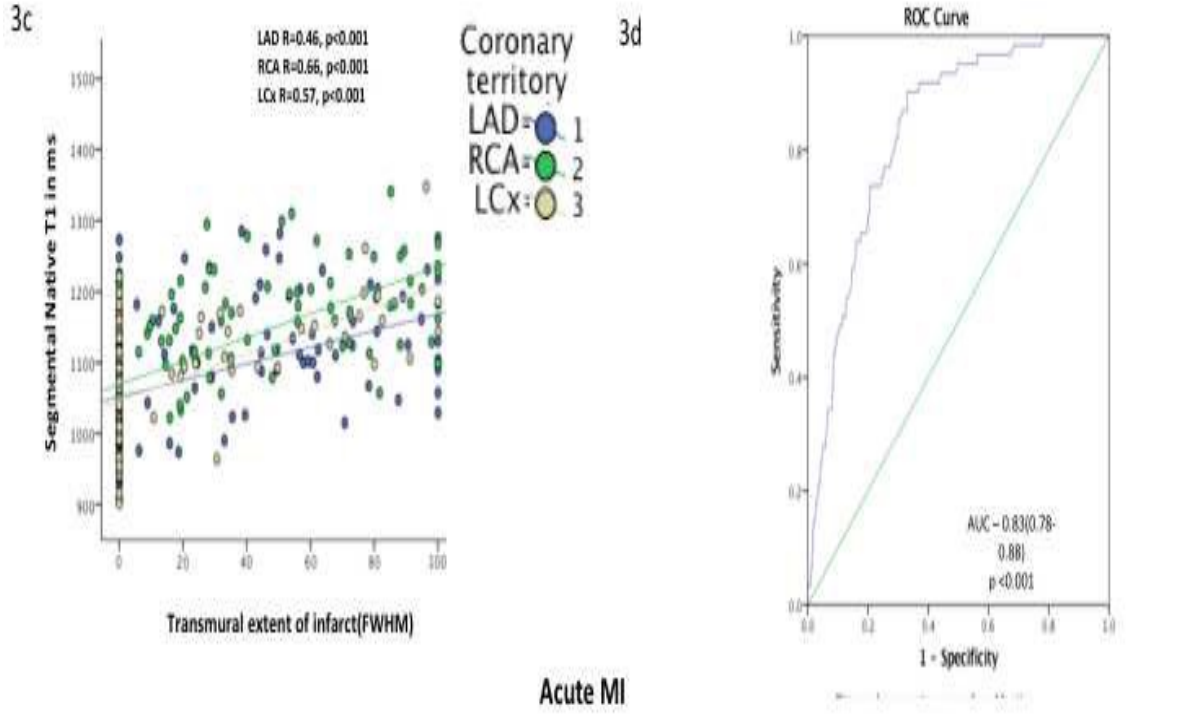


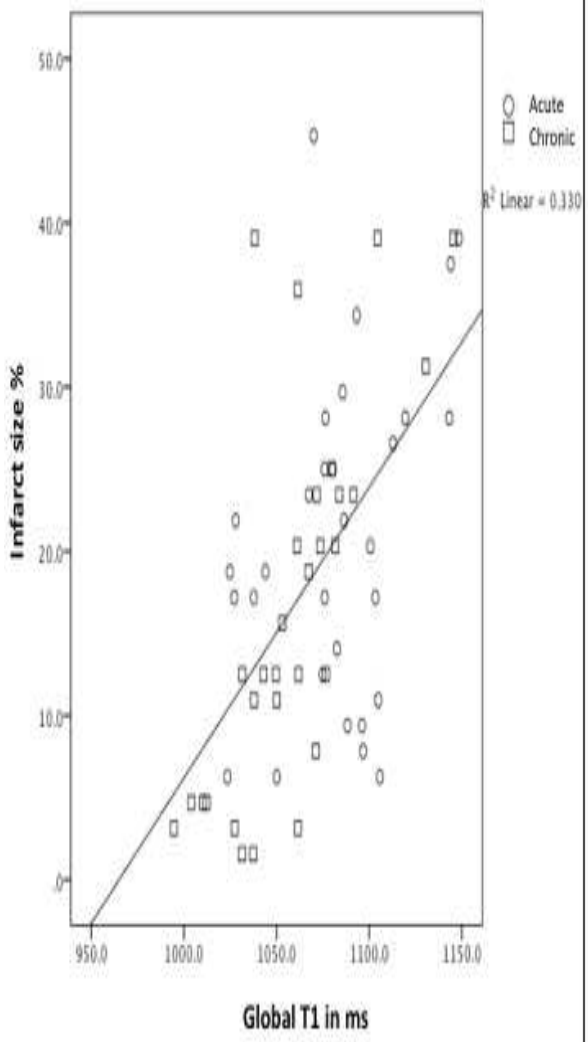
Chronic MI


3a
R=0.57, p<0.001
Segmental Native T1 in ms
Transmural extent of infarct (FWHM)
3b
*p<0.01
Segmental Native T1 in ms
No LGE
LGE + Viable TEI <75%
LGE + Non-viable TEI ≥75%


3c
LAD R=0.46, p<0.001
RCA R=0.66, p<0.001
LCx R=0.57, p<0.001
Coronary territory
LAD = 1
RCA = 2
LCx = 3
Segmental Native T1 in ms
Transmural extent of infarct(FWHM)
3d
ROC Curve
Sensitivity
1 - Specificity
AUC = 0.83(0.78-0.88)
p <0.001

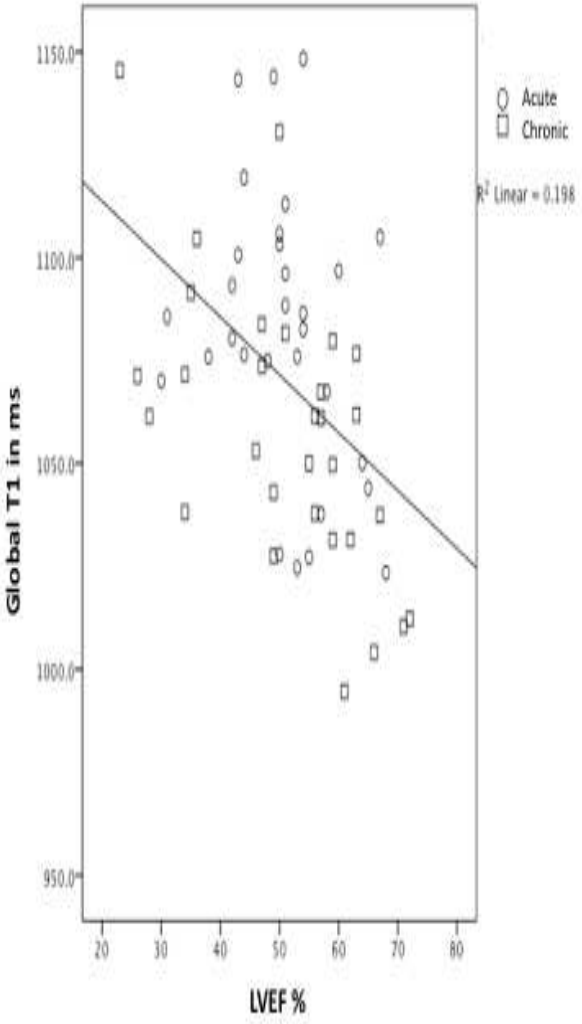
Acute MI

Figure 4a: Global T1 vs Infarct size



	R value	P-value
Total cohort (n=60)	0.575	<0.001
Acute STEMI (n=30)	0.365	0.048
Chronic MI (n=30)	0.717	<0.001

Figure 4b: Global T1 vs LVEF



	R value	P-value
Total cohort (n=60)	-0.445	<0.001
Acute STEMI (n=30)	-0.291	0.118
Chronic MI (n=30)	-0.596	<0.001

Figure: Global native T1 in Acute MI, chronic MI and normal volunteer